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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/533,547	03/23/2000	Randall S. Kent	JAO 28796.02	3851

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EXAMINER	
MCKANE, ELIZABETH L	
ART UNIT	**PAPER NUMBER**
1744	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/533,547	KENT ET AL.	
	Examin r	Art Unit	
	Leigh McKane	1744	

-- Th MAILING DATE of this communication appears on the cover she t with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,30,34,36-83 and 173-196* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28,30,34,36-83 and 173-196* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claim Objections

1. Claims 183, 185, and 187 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Specifically, the above claims recite a dose rate of "about 2.0 kGy/hr" but all depend from a claim which recites a dose rate of "about 3.0 kGy/hr". If the dose rate is "about 3.0 kGy/hr," it is not properly limited by a dose rate of "about 2.0 kGy/hr," unless Applicant considers "about 2.0 kGy/hr" to be "about 3.0 kGy/hr." Thus, for purposes of this rejection, the Examiner will treat a recitation of "about 3.0 kGy/hr" to include rates of "about 2.0 kGy/hr."

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 5, 13-15, 18, 20-22, 25-28, 30, 34, 37, 45-47, 50, 52-54, 57, 60, 68, 70, 73, 75-77, 80-83, 176, and 179 are rejected under 35 U.S.C. 102(b) as being anticipated by Sakai et al.

Sakai et al teaches the sterilization of enzymes containing glucose and/or lactose (food ingredients) and L-cysteine, an anti-oxidant protectant. The enzyme preparations are sterilized in lyophilized form with gamma radiation at a dose rate of 3.45 rad/hr (0.345 kGy/hr). Enzymes

are a proteinaceous material and both glucose and lactose are both carbohydrates. See pages 1130-1131. As Sakai et al discloses that the gamma radiation source is Co^{60}, the dose rate is inherently "not constant for the duration of the sterilization procedure" since Co^{60} experiences natural decay over the duration of the procedure, the decay reducing the dose rate.

4. Claims 1, 2, 4-8, 14, 19, 21, 22, 25-28, 30, 34, 36-40, 46, 51, 53, 54, 57, 59-63, 69, 74, 76, 77, 80-83, 177, 180, 188-196 are rejected under 35 U.S.C. 102(b) as being anticipated by Chanderkar et al.

Chanderkar et al teaches sterilization of fibrinogen in lyophilized form. The preparation is irradiated by gamma radiation with a dose rate of 12,500 R/min (7.5 kGy/hr) at a temperature of 0-4 °C. Potassium iodide, an electron scavenger, is added as a protectant. See pages 283-284. As Chanderkar et al discloses that the gamma radiation source is Co^{60}, the dose rate is inherently "not constant for the duration of the sterilization procedure" since Co^{60} experiences natural decay over the duration of the procedure, the decay reducing the dose rate.

5. Claims 1, 2, 4-6, 9, 14, 18, 20-23, 25-28, 182, 183 rejected under 35 U.S.C. 102(b) as being anticipated by Baquey et al.

Baquey et al teaches the use of gamma radiation to sterilize albumin coated upon polyester. The samples were lyophilized and irradiated at a dose rate of 2600 rad/min (1.56 kGy/hr) in a low oxygen atmosphere (nitrogen). See page 186. Baquey et al is silent with respect to adding a sensitizer to the biological material before irradiation. As a rate of 1.56 kGy/hr is "about 2.0 kGy/hr" it is also "about 3.0 kGy/hr" as defined by Applicant. As Baquey et al discloses that the gamma radiation source is Co^{60}, the dose rate is inherently "not constant

for the duration of the sterilization procedure" since Co^{60} experiences natural decay over the duration of the procedure, the decay reducing the dose rate.

6. Claims 1, 2, 5, 10, 14, 19, 22, and 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Field et al.

Field et al teaches the sterilization of brain tissue that has been lyophilized. The tissue is irradiated with gamma radiation at a dose rate of 43,000 rad/min (25.8 kGy/hr). As Field et al discloses that the gamma radiation source is Co^{60}, the dose rate is inherently "not constant for the duration of the sterilization procedure" since Co^{60} experiences natural decay over the duration of the procedure, the decay reducing the dose rate.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 3, 58, 173-175, 177, and 178 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai in view of Horowitz et al.

With respect to claims 3 and 58, Sakai et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it

would have been further obvious to remove the solvent before irradiation, in the manner of Sakai et al.

As to claims 173-175, Sakai et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the enzyme in the method of Sakai et al, in order to increase sterilization effectiveness.

With respect to claims 177 and 178, the stabilizer employed by Sakai et al (L-cysteine) is not the same as that claimed by the instant invention. Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use stabilizer of Horowitz et al in place of that of Sakai et al.

9. Claims 4, 6, 11, 12, 16, 17, 36, 38, 43, 44, 48, 49, 59, 66, 67, 71, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al.

Sakai et al teaches generally the sterilization of "biological materials" and specifically teaches the sterilization of an enzyme, trypsin. Although trypsin is not a component of blood, blood does contain other enzymes. Thus, it would have been obvious to one of ordinary skill in the art to use the method of Sakai et al to sterilize other enzymes and biological materials since

the method has been shown to be effective and since Sakai et al discloses that "the biological activities of these drugs are not impaired and undesirable byproducts are not formed."

10. Claims 58, 173, and 175 rejected under 35 U.S.C. 103(a) as being unpatentable over Chanderkar et al in view of Horowitz et al.

With respect to claim 58, Chanderkar et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Chanderkar et al.

As to claims 173 and 175, Chanderkar et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the enzyme in the method of Chanderkar et al, in order to increase sterilization effectiveness.

11. Claims 3, 30, 34, 36-38, 41, 46, 50, 52-61, 64, 69, 73, 75-83, 173-181, 184-187 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baquey et al in view of Horowitz et al.

With respect to claims 3 and 58, Baquey et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches

that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Baquey et al.

As to claims 30, 34, 36-38, 41, 46, 50, 52-55, 57, 59-61, 64, 69, 73, 75-78, 80-83, and 184-187, Baquey et al fails to disclose using a stabilizer in the gamma sterilization of lyophilized albumin. Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use stabilizer of Horowitz et al in the method of Baquey et al.

With respect to claims 173-181, Baquey et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological materials wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the albumin in the method of Baquey et al, in order to increase sterilization effectiveness.

With respect to claims 56 and 79, in order to achieve a low oxygen atmosphere, Baquey et al uses an inert gas, nitrogen. Although Baquey et al doesn't disclose argon as the inert gas, it is deemed obvious to substitute one inert gas for another in the method of Baquey et al.

12. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baquey et al.

In order to achieve a low oxygen atmosphere, Baquey et al uses an inert gas, nitrogen. Although Baquey et al doesn't disclose argon as the inert gas, it is deemed obvious to substitute one inert gas for another in the method of Baquey et al.

13. Claims 3, 30, 34, 37, 42, 46, 51, 57, 58, 60, 65, 69, 74, 77, 80-83, 173-181 are rejected under 35 U.S.C. 103(a) as being unpatentable over Field et al in view of Horowitz et al.

et al fails to disclose using a stabilizer.

With respect to claims 3 and 58, Field et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Field et al.

As to claims 30, 34, 37, 42, 46, 51, 57, 60, 65, 69, 74, 77, 80-83, and 176-181, Field et al is silent as to using a stabilizer. Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use stabilizer of Horowitz et al in the method of Field et al.

With respect to claims 173-175, Field et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological materials

wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the tissue in the method of Field et al, in order to increase sterilization effectiveness.

Response to Arguments

14. Applicant's arguments filed 2 October 2003 have been fully considered but they are not persuasive.

Applicant argues that to be consistent with the specification, "the term "not constant" must indicate a variation in the rate of irradiation that is greater than that resulting from natural decay of the source material over the duration of the sterilization procedure." See page 24 of the Response. However, the specification provides no guidance whatsoever as to how this term is to be construed. Although Applicant points to the only place (page 14, lines 10-12) in the specification that could even remotely yield an interpretation of "not constant," there is certainly no indication that "not constant" must mean an increasing rate. As the term is nowhere defined by the specification, it is unclear how Applicant can attest that the Examiner's definition is inconsistent with the specification. If Applicant intends for "not constant" to mean a rate other than the naturally decreasing rate caused by source decay, it must be defined by the specification so as to leave no room for conjecture.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 703-305-3387 until December 15, 2003. After December 15, 2003 the examiner can be reached at 571-272-1275. The examiner can normally be reached on Monday-Wednesday (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 703-308-2920 or at 571-272-1281 after December 15, 2003. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Leigh McKane
Primary Examiner
Art Unit 1744

elm
17 November 2003